



Chronic Cholestatic liver Disease

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By the end of this lecture the student will be able to:

- Explain the pathogenesis ,pathologic features and complications of chronic cholestatic liver disease (primary biliary cholangitis , primary sclerosing cholangitis and secondary biliary cirrhosis)
- Correlate pathologic features of common chronic cholestatic liver diseases with their clinical picture ,investigations and complications

Lecture Plan



1. Part 1 (5 min) Features of cholestatic liver disease
2. Part 2 (15 min)Primary biliary cholangitis
3. Part 3 (15 min) Primary sclerosing cholangitis
4. Part 4 (10 min) Causes of secondary biliary cirrhosis & comparison
5. Lecture Quiz (5 min)

REMINDER

Causes of Chronic Hepatitis (cont.)

- ✓ **1-Viral hepatitis**
- ✓ **2-Auto Immune Hepatitis**
- ✓ **3-Alcoholic & non Alcoholic FLD
/Hepatitis**
- ✓ **4-Drug Induced Hepatitis**

5-Cholestatic liver disease

6-Wilson's Disease

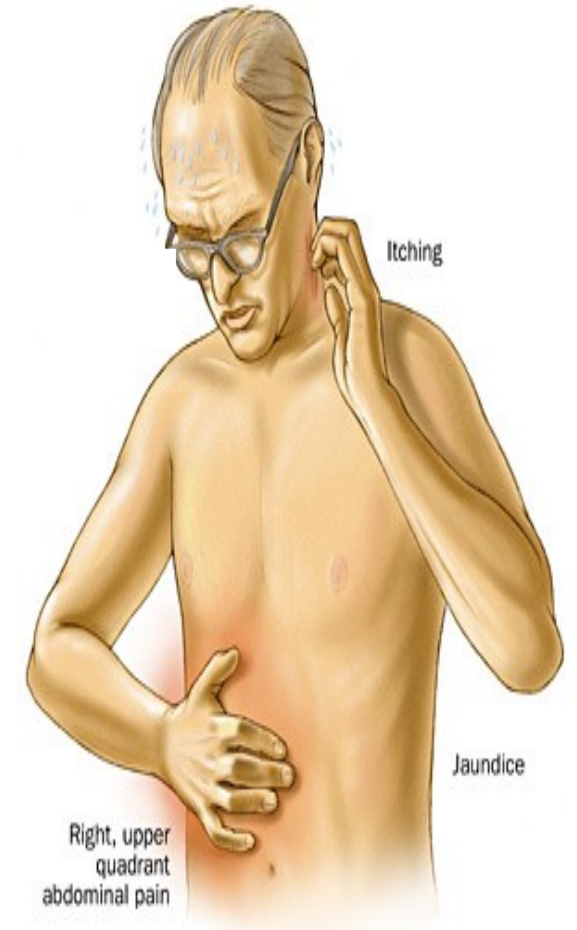
7-Alpha 1 antitrypsin Deficiency

} Discussed in another
discipline

5. Cholestatic Liver Diseases



- Jaundice
- Pruritus
- Dark urine - Light stools
- LAB: marked increase in
 - ALKALINE PHOSPHATASE &
 - GGT (Gamma-Glutamyl Transpeptidase)

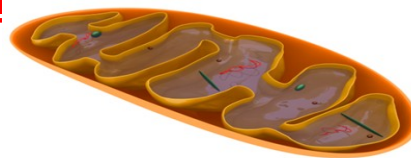


5a-Primary Biliary Cholangitis / Cirrhosis

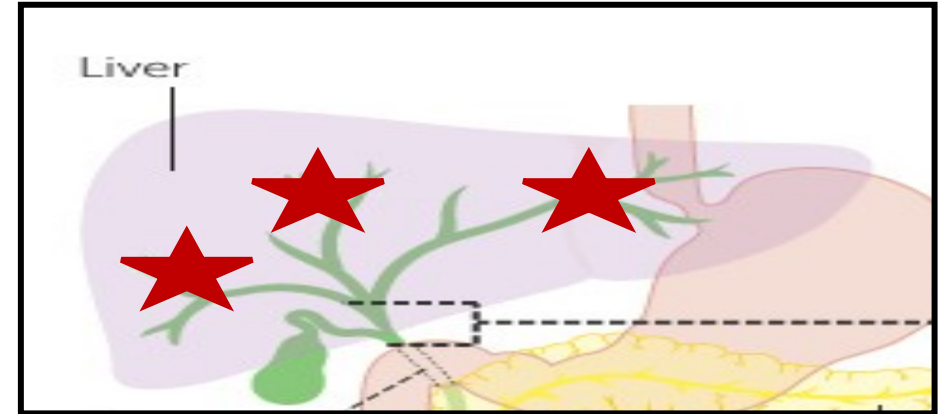


Pathogenesis :

- **Autoimmune disease causing**
- **Non-suppurative**
destruction of small and medium-sized
INTRAHEPATIC BILE DUCTS.
- **Increased titre of antimitochondrial antihodv (AMA)**
- **Common in middle-agea**
women



GIT & Metabolism



https://upload.wikimedia.org/wikipedia/commons/thumb/1/1d/Diagram_showing_the_position_of_the_perihilar_bile_ducts_CRUK_357.svg/250px-Diagram_showing_the_position_of_the_perihilar_bile_ducts_CRUK_357.svg.png



**bile duct
epithelium**

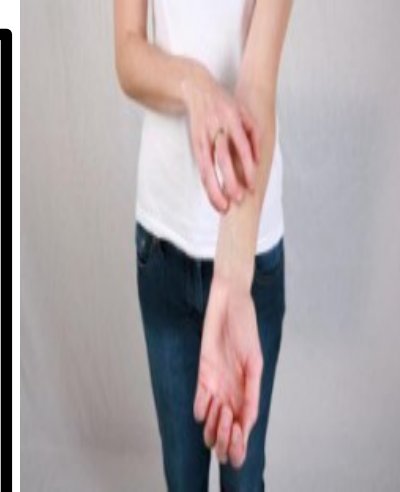
https://www.google.com/search?biw=1536&bih=754&tbm=isch&sxsr=ACYBGNR_wezSCJN8rtRy7hQXddkDXuKMqA%3A1569494315377&sa=1&ei=K5WMXbHaFo6pgAbI4rHAAG&q=mitochondria+diagram+no+labels&oq=mitochondria+diagram+no+labels&gs_l=img.12...14254.18643..20316...0.0..0.123.1143.0j10.....0....1..gws-wiz-img.....0i67j0.TRLjzvK5qSI&ved=0ahUKEwjxm5T5pe7kAhWOFMAKHUhxDCgQ4dUDC6Ac#imgsrc=ZS0ondDyylUyM:

Primary Biliary Cholangitis /Cirrhosis



C/P

- **Jaundice**
- **Pruritus**
- Palpebral **Xanthomas** due to hypercholesterolemia
- **Associated with autoimmune diseases as Sjogren's Syndrome & Rheumatoid arthritis**



<https://pancreaticcanceraction.org/wp-content/uploads/2012/10/itching-300x2051-250x170.jpeg>



<https://hlives.com/content/images/size/w600/2018/11/Jaundice--Icterus--Types--Causes--Symptoms--Diagnosis--Treatment---Prevention.jpg>



<https://img.medscapestatic.com/pi/meds/ckb/69/60669tn.jpg>

Primary Biliary Cholangitis /Cirrhosis

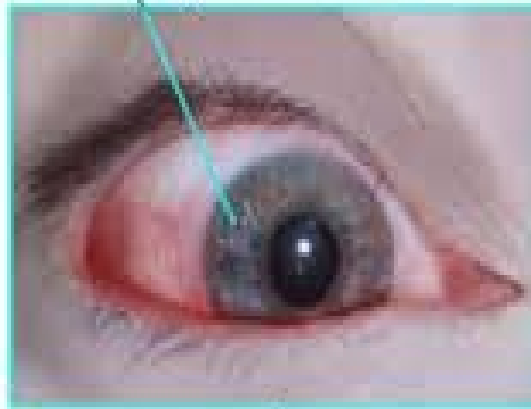


Examples of **autoimmune** diseases that

Sjogren's

Syndrome

Dry eyes,
damage to
eye surface



Dry mouth,
increased
tooth decay



Rheumatoid



<https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcQVX2NIwFBPcXxln6hF4HKXbbASZ7sCtwH9WjY0X0Tvr0guknPI>

https://ubmidrupalcandd.s3-eu-west-1.amazonaws.com/styles/article_image_620x420/s3/public/CD%20Image%20Library/Editorial/Clinical/General%20clinical/shutterstock_504533113%20rheum%20hand.jpg?itok=qGQYt7KV

Primary Biliary Cirrhosis



Gross: Deep green in colour
micronodular cirrhosis



<https://i2.wp.com/dailymedfact.com/wp-content/uploads/2019/02/PBC.jpg?fit=1093%2C627&ssl=1>



<https://slideplayer.com/slide/7904085/25/images/12/Common+Final+Pathway%3A+Biliary+Cirr>

Primary Biliary Cholangitis /Cirrhosis

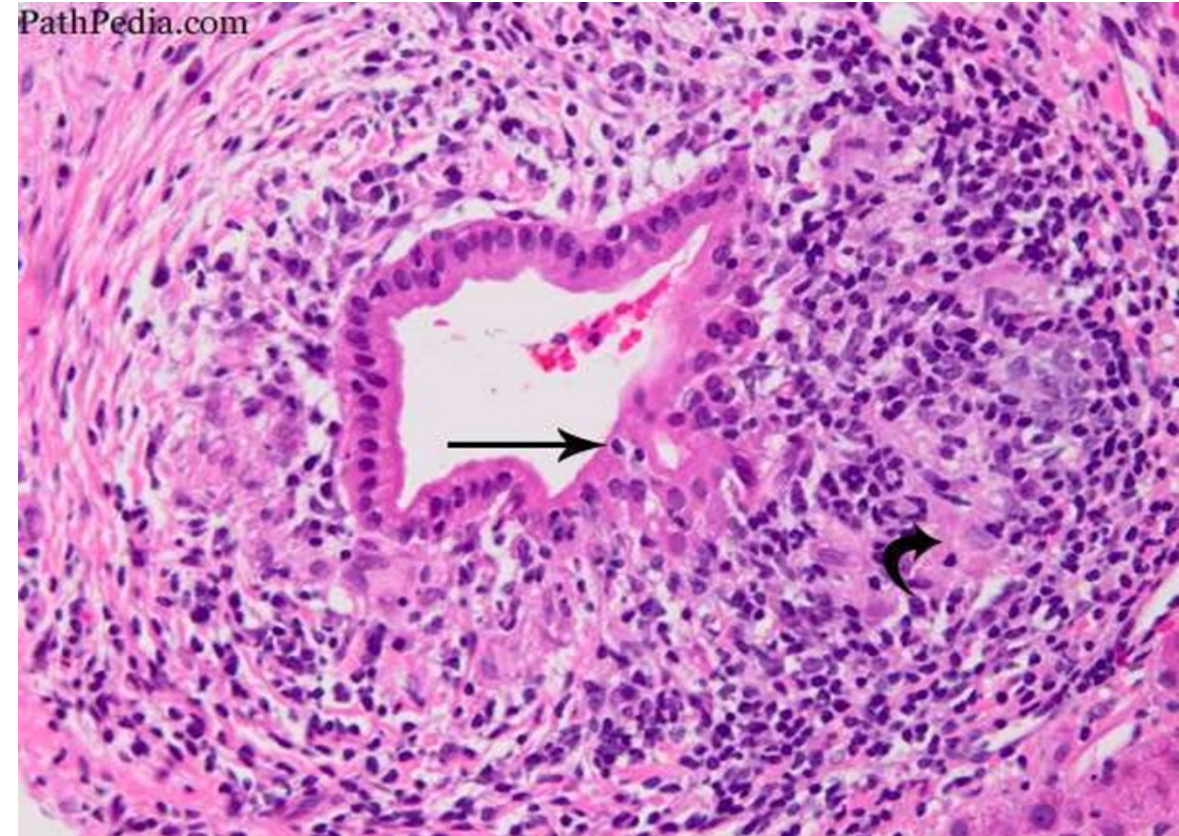


Mic :

1. Florid duct lesion

- Interlobular bile duct destruction by lymphocytes & plasma cells +/- granuloma
- Periportal cholestasis ,interface hepatitis.

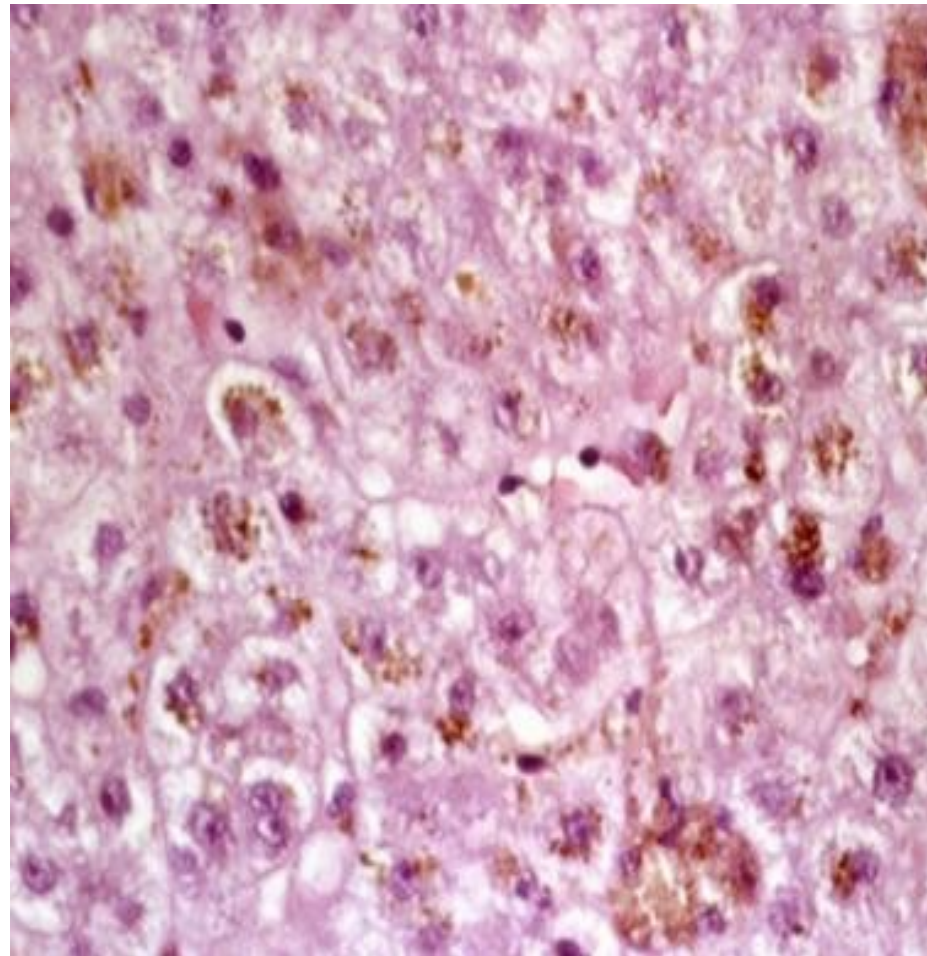
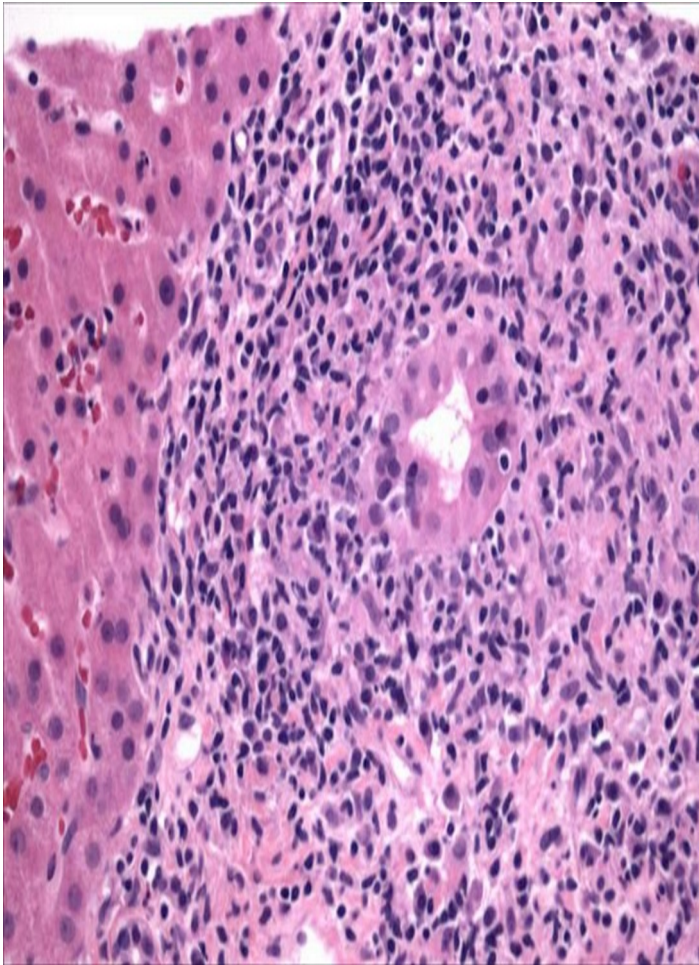
2. Ductopenia



Granuloma + bile duct injury by lymphocytes

[https://www.pathpedia.com/education/eatlas/histopathology/liver_and_bile_ducts/primary_biliary_cirrhosis_\(pbc\)/primary-biliary-cirrhosis-pbc-2-li066-1.jpeg?Width=600&Height=450&Format=4](https://www.pathpedia.com/education/eatlas/histopathology/liver_and_bile_ducts/primary_biliary_cirrhosis_(pbc)/primary-biliary-cirrhosis-pbc-2-li066-1.jpeg?Width=600&Height=450&Format=4)

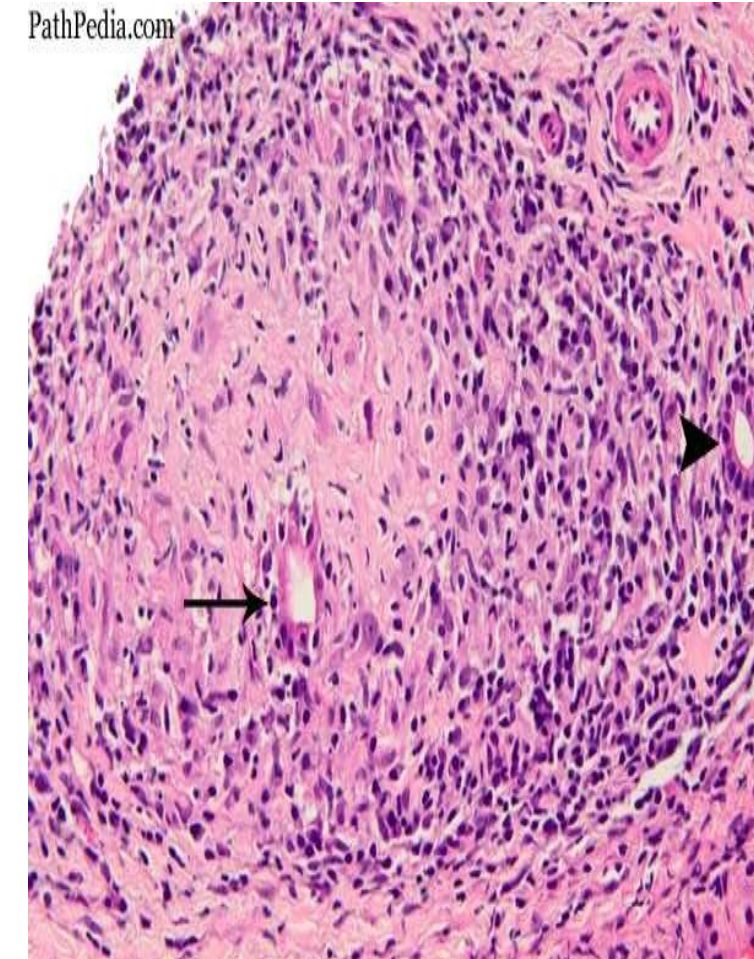
Primary Biliary Cholangitis /Cirrhosis



Portal inflammation & cholestasis in hepatocytes

<https://d1yboe6750e2cu.cloudfront.net/i/8e2e0a54b0ef989f17c785ff31c47395c9bf118b>

<https://www.medicinesstatic.com/pi/meds/ckb/46/35346tn.jpg>



Ductopenia

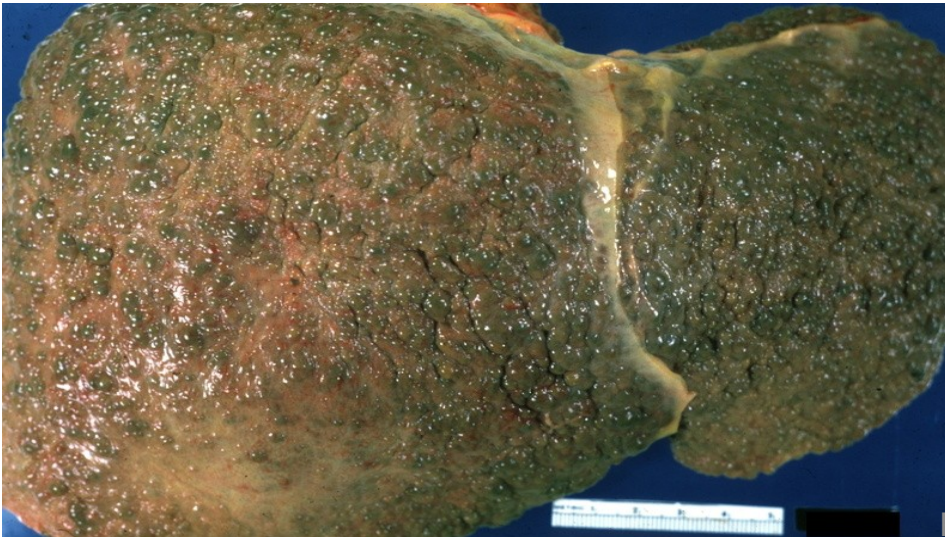
[https://www.pathpedia.com/education/eatlas/histopathology/liver_and_bile_ducts/primary_biliary_cirrhosis_\(pbc\)/primary-biliary-cirrhosis-pbc-5-li055-2.jpeg?Width=600&Height=450&Format=4](https://www.pathpedia.com/education/eatlas/histopathology/liver_and_bile_ducts/primary_biliary_cirrhosis_(pbc)/primary-biliary-cirrhosis-pbc-5-li055-2.jpeg?Width=600&Height=450&Format=4)

Primary Biliary Cholangitis / Cirrhosis



Fate (complications)

- Severe portal hypertension > variceal bleeding + hepatic encephalopathy
- Cirrhosis



Primary biliary cholangitis (Quiz)



Primary biliary cholangitis is due to which of the following ?

- a) Accumulation of fat inside hepatocytes
- b) Autoimmune disease against hepatocytes
- c) Excessive Alcohol intake
- d) Autoimmune destruction intrahepatic bile ducts

Primary biliary cholangitis (Quiz)



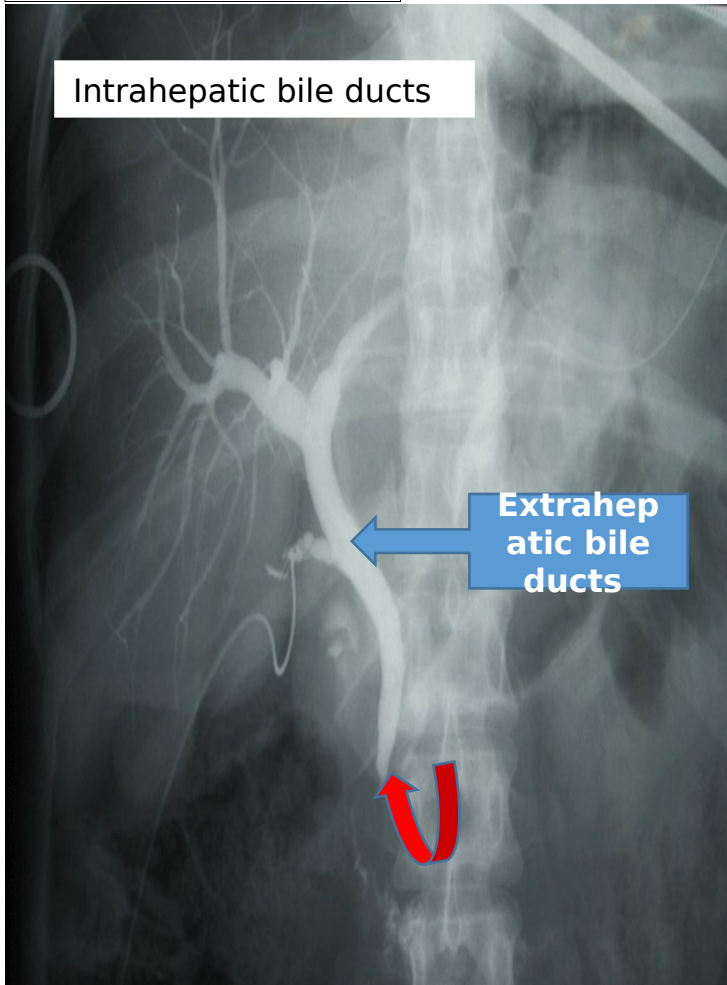
Primary biliary cholangitis is due to which of the following ?

- a) Accumulation of fat inside hepatocytes
- b) Autoimmune disease against hepatocytes
- c) Excessive Alcohol intake
- d) Autoimmune destruction intrahepatic bile ducts

Compare



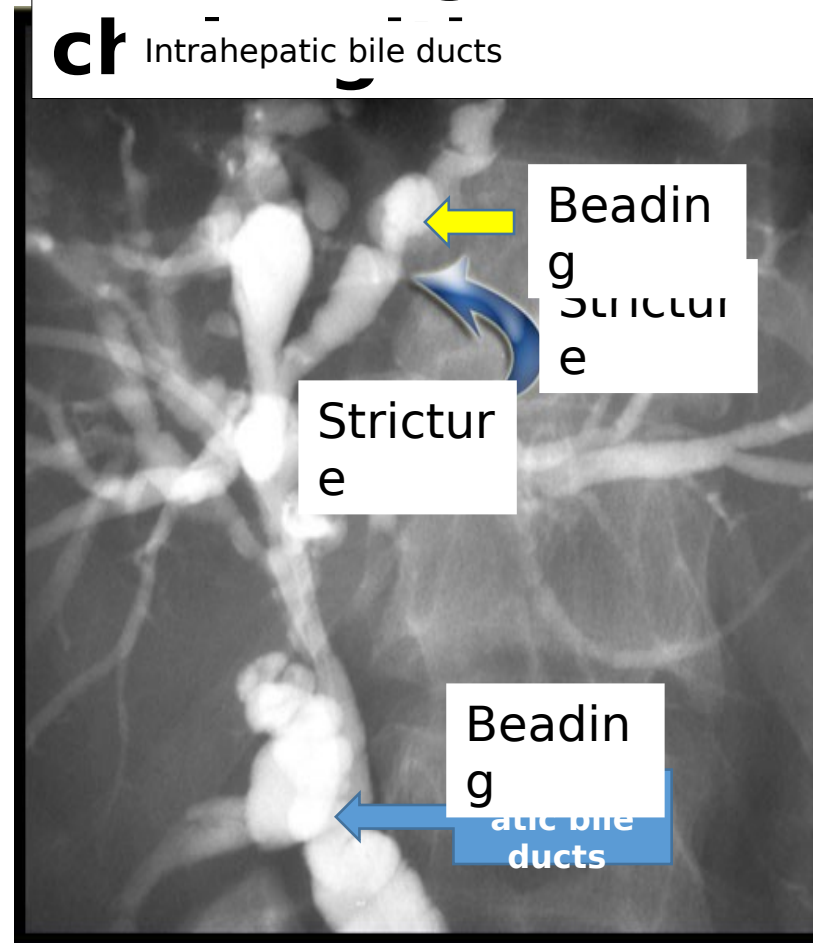
Normal



9/19/24

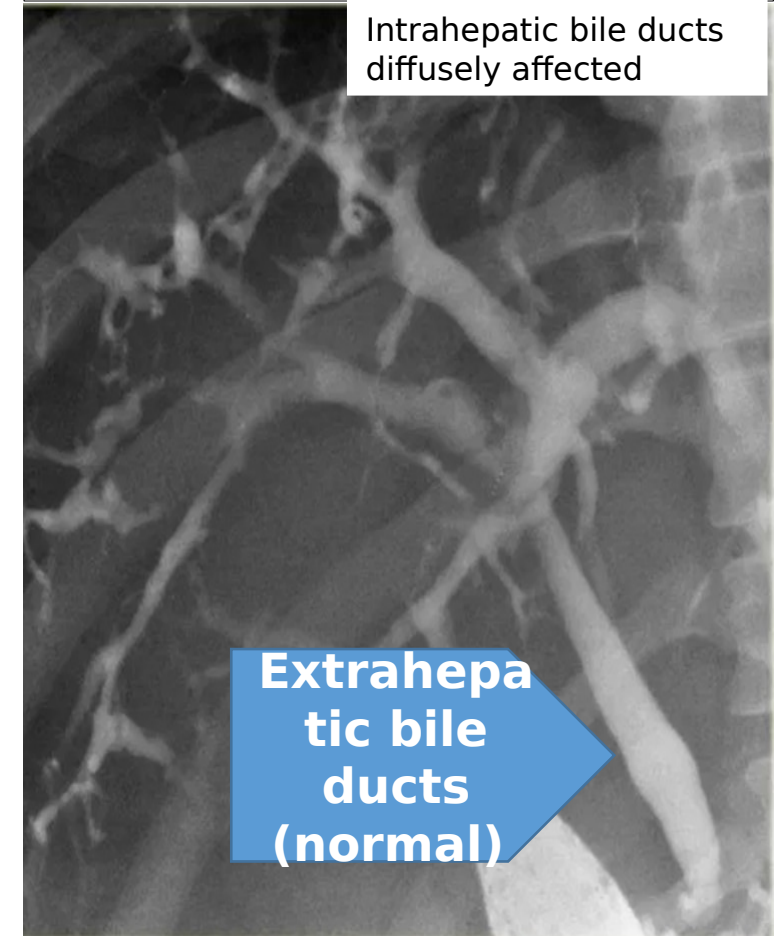
Primary sclerosing

cholangitis



http://www.radiologyassistant.nl/data/bin/a50979796b82f9_Afbeelding-8.jpg

Primary biliary cholangitis



<https://i2.wp.com/dailymedfact.com/wp-content/uploads/2019/02/PBC.jpg?fit=1093%2C627&ssl=1>

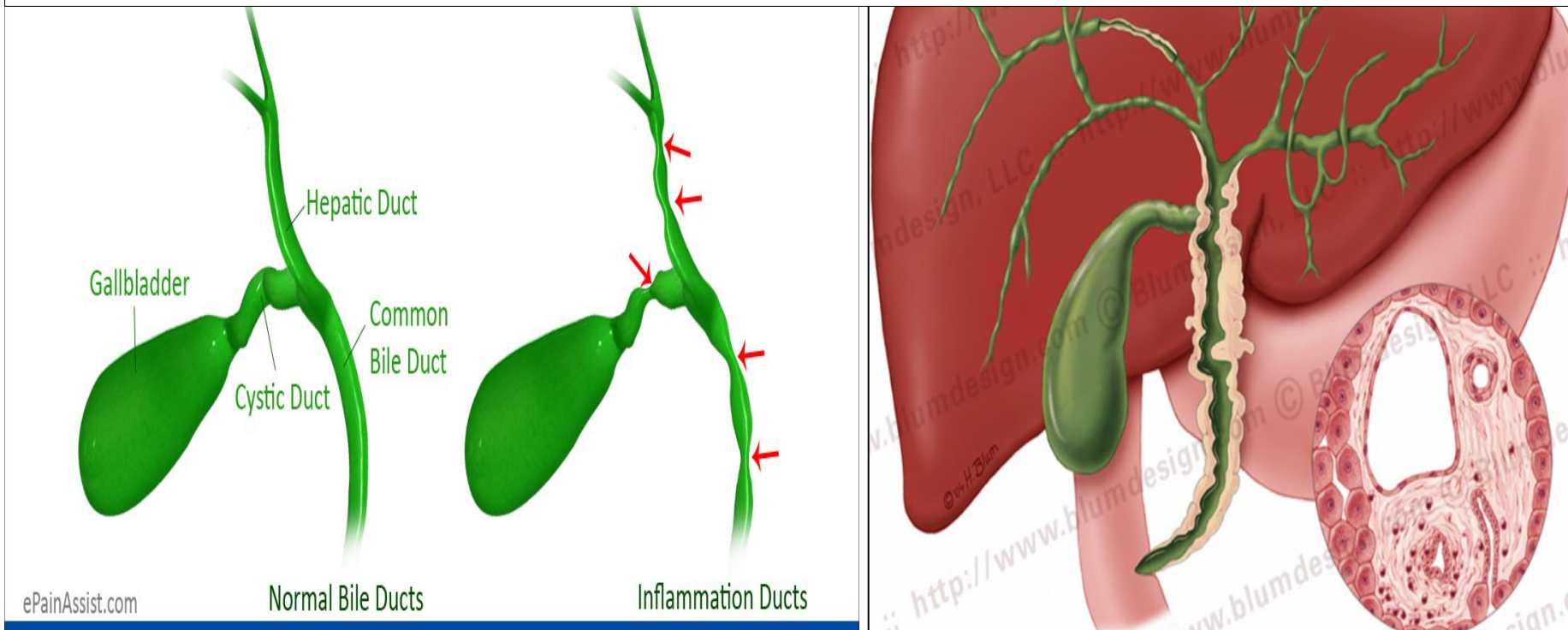
15

5b-Primary Sclerosing Cholangitis (PSC)



Def:

Progressive PATCHY fibrosis & destruction of extrahepatic & intrahepatic bile ducts of all sizes



5b-Primary Sclerosing Cholangitis (PSC)



Pathogenesis:

- Immunologically mediated
- Chronic progressive disease
- fibrosis & destruction of

- **extrahepatic & intrahepatic bile ducts of all sizes**

Fate:

- **Cirrhosis**
- **Cholangiocarcinoma**

- **Males (2:1)**
- **Associated With Ulcerative colitis**
- **+ve ANCA (Anti-neutrophil cytoplasmic) AB**



5b-Primary Sclerosing Cholangitis (PSC)



ERCP:

- Patchy lesion of extrahepatic & intrahepatic ducts
- Beading due to
 - Narrow strictures
 - Alternating with normal or dilated ducts



<https://qph.fs.quoracdn.net/main-qimg-5f5cd10f2c4e6ff83d9887bd15280943.webp>

:endoscopic retrograde cholangiopancreatography

5b-Primary Sclerosing Cholangitis(PSC)



Mic:

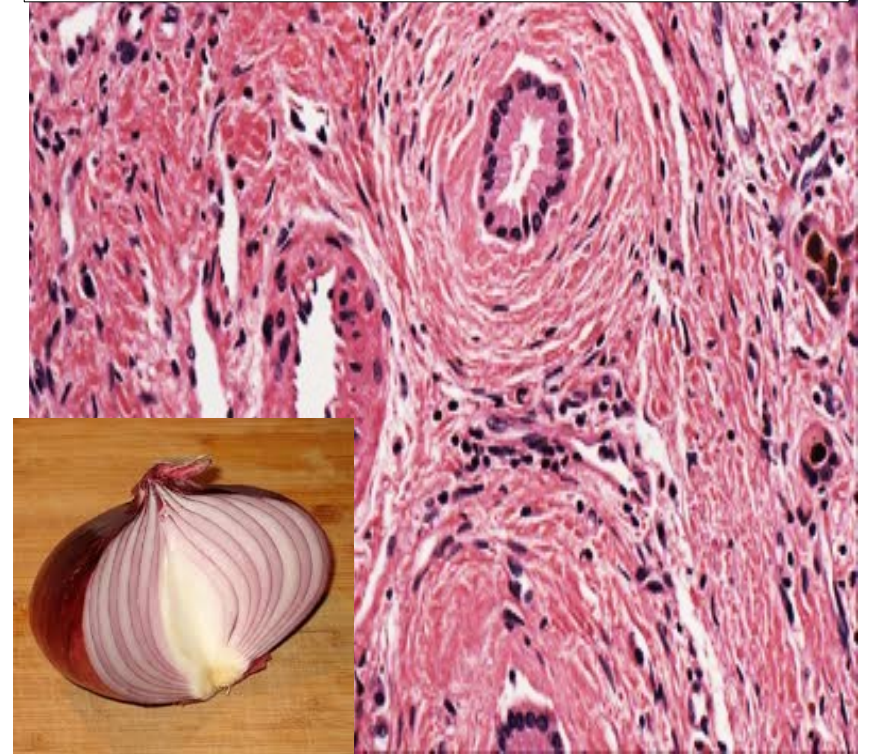
Large ducts :

- Chronic inflammation
- Narrowing of lumen

Small ducts

- **Circumferential fibrosis = onion skin fibrosis** > lumen disappears

circumferential
fibrosis

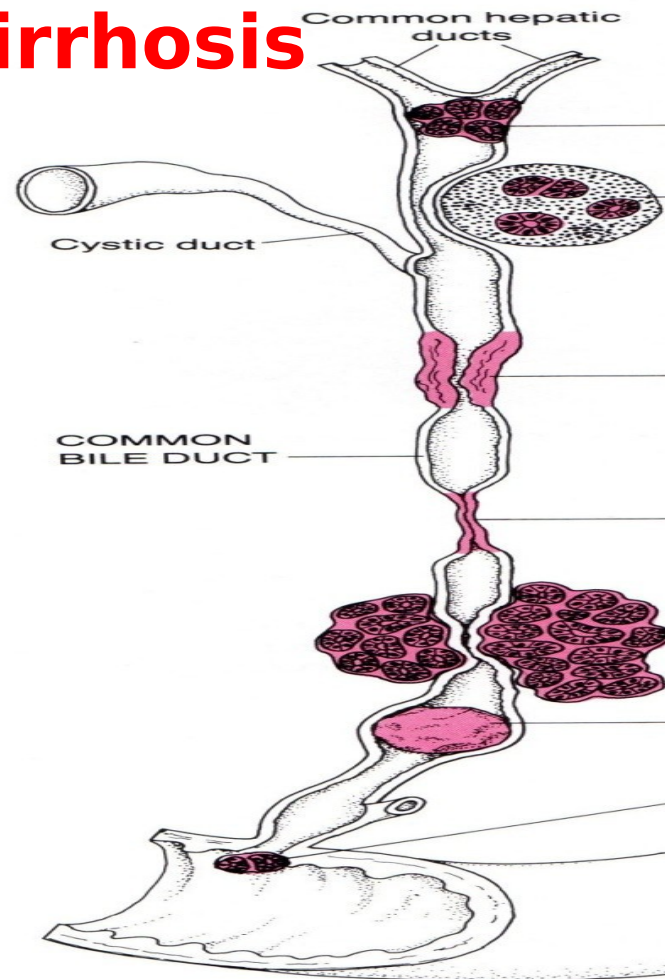


<https://img.medscapestatic.com/fullsize/migrated/552/500/mgm552500.fig3.gif19>

5c.Secondary Biliary Cirrhosis



Causes of secondary biliary obstruction leading to cholangitis & cirrhosis



Bile Duct Carcinoma

Enlarged Lymph

postoperative

Congenital Biliary

Pancreatic Carcinoma

Gall Stone

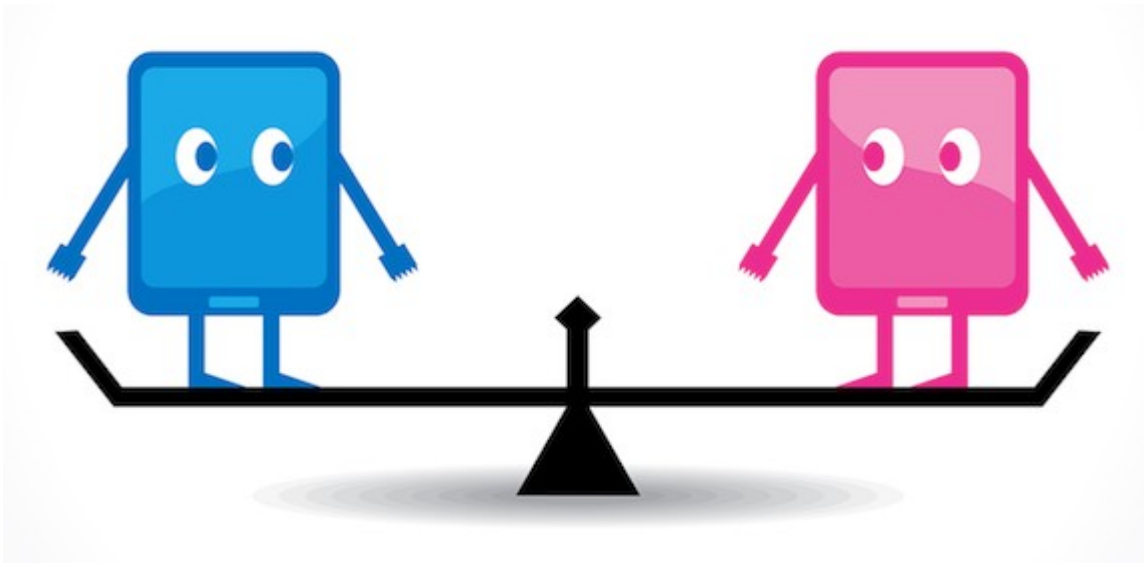
Carcinoma of ampulla
of vater

FIGURE 14-27
Major causes of extrahepatic biliary obstruction.

Primary Cholangitis (Quiz)



Compare between primary biliary cholangitis & primary sclerosing cholangitis



Primary Cholangitis (Quiz)

	PBC	PSC
Gender		
Type of lesion its site		
Ducts		
Assoc with		
Abs		
Diagnosed by		
Mic		
Fate		

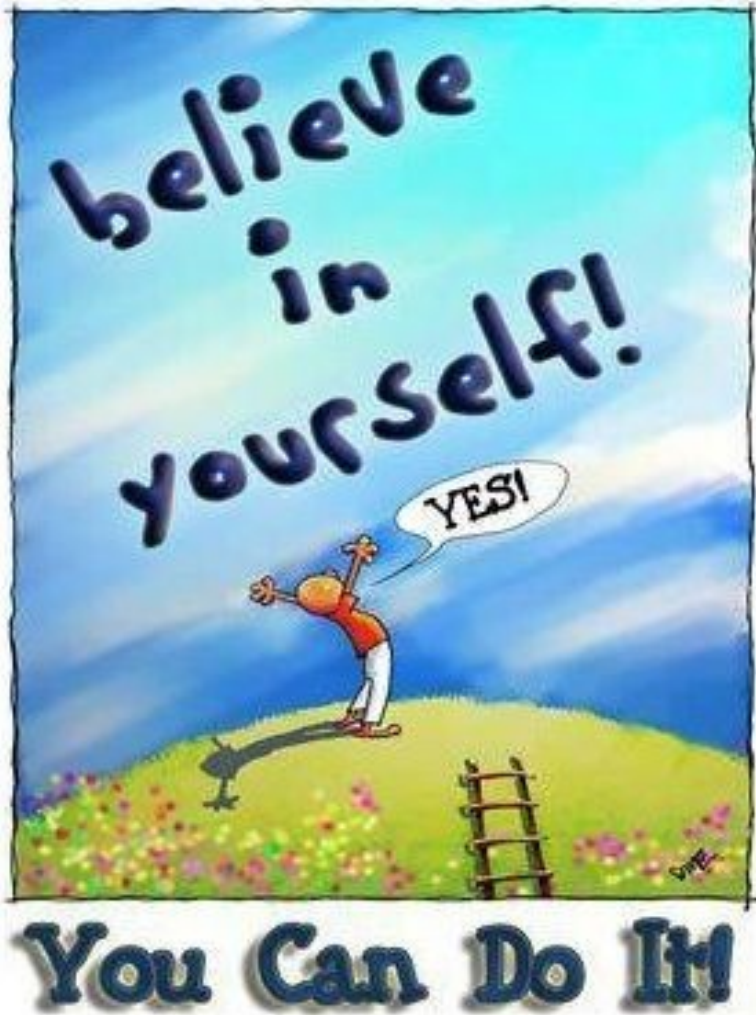
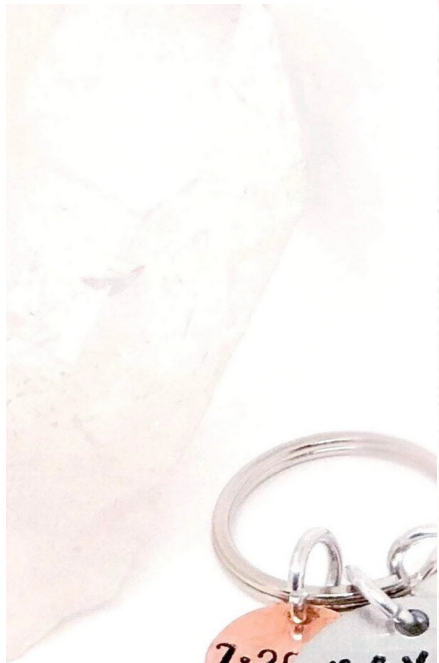
PBC Versus PSC



	Primary biliary cholangitis	Primary sclerosing cholangitis
Gender	>in female	> in male
Type of lesion its site	Florid duct inflammation +/-granuloma	<ul style="list-style-type: none"> inflammation in large extrahepatic FIBROSIS in small ducts
Ducts	small & medium-sized intrahepatic bile ducts.	all ducts(intra& extra ,small & large)
Associated with	Sjogren's scleroderma - rheumatoid	Ulcerative colitis
Antibodies	AMA	ANCA
Diagnosed by	biopsy	ERCP beading
Mic	-Florid duct lesion -Ductopenia	onion skin fibrosis >dense
Fate	cirrhosis	Cirrhosis/ cholangiocarcinoma



- Cholestatic liver disease may be primary or secondary
- Primary biliary cholangitis is autoimmune destruction intrahepatic bile ducts
- Primary sclerosing cholangitis is chronic progressive disease fibrosis & destruction of extrahepatic & intrahepatic bile ducts of all sizes
- Secondary biliary cirrhosis is due to obstruction of extrahepatic biliary tract by stone , tumour ,LN etc



we 😊
believe
in you

Suggested Textbooks



Neil D. Theise. Liver and gall bladder. In Robbins and Cotran
pathologic basis of disease, 10th edition. Kumar, Abbas &
Aster (eds). Elsevier Saunders. Pages 637-676